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APPLICATION NO	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO	CONFIRMATION NO.
09/996,738	11/30/2001	Philip Gotwals	A076 US	4464

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EXAMINER
HADDAD, MAHER M

ART UNIT	PAPER NUMBER
1644	9

DATE MAILED: 07/14/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Application No.	Applicant(s)
09/996,738	GOTWALS ET AL.
Examiner	**Art Unit**
Maher M. Haddad	1644

Office Action Summary

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 April 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☐ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4)☐ Interview Summary (PTO-413) Paper No(s). _____.
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other: .

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 4/29/03(Paper No. 8), is acknowledged.

2. Claims 1-7 are pending and currently under consideration.

3. The following new ground of rejection is necessitated by the amendment filed on 4/29/03, paper No. 8.

4. The following is a quotation of the second paragraph of 35 U.S.C. 112.

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention

5. Claim 1-7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claim 1 is indefinite in the recitation of "the epitope comprises amino acid residues 91-96 of Figure 15 (SEQ ID NO:8)", because SEQ ID NO: 8 consisting of only 6 amino acids sequence. It is unclear how amino acid residues 91-96 are encompassed by SEQ ID NO:8. Furthermore, Figure 15 is represented by SEQ ID NO:6.

6. In view of the amendment filed on filed 4/29/03(Paper No. 8), only the following rejections remained.

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

8. Claim 1-6 stand rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent No. 5,788,966 (IDS Ref. No. AA) for the same reasons set forth in the previous Office Action, paper No. 6, mailed 2/11/03.

Applicant's arguments, filed 4/29/03 (Paper No. 8), have been fully considered, but have not been found convincing.

Applicant argues that '966 patent discloses that mAb 1B3.1 "reacts with T cells which have been activated for prolonged periods, both in vitro an din vivo" (col., 7, lines 52-54). Applicant argues the '966 patent discloses that the VAL-1 molecule may participate in the compartmentatization of activated T cells to sites of tissue localized immune responses such as those occurring in the synovial (col., 9, lines 3-6). Further, the '966 patent discloses that the synovial fluid of arthritis patients expresses enhanced levels of VLA-1 (col. 8, lines 67-68). Applicant argues that there is no disclosure in the '966 patent that of mAb binding to an epitope of VLA-1 comprising amino acid residues 91-96 of Figure 15 to provide a decrease in arthritic score of about 65% or greater when compared to a control antibody treated subject. Applicant argues that mAb 1B3.1 affects the interaction of VLA-1 and T cells in conditions where enhanced levels of VLA-1 are noted does not disclose binding of mAb's to an epitope of VLA-1 comprising amino acid residues 91-96 of Figure 15 to provide a decrease in arthritic score of about 65% or greater when compared to a control antibody treated subject.

Applicant argues that the burden is not on the Applicants to show that the '966 patent mAb 1B3.1 could not under any circumstances target amino acid residues 91-96 of Figure 15 to provide a decrease in arthritic score of about 65% or greater when compared to a control antibody treated subject. Applicant argues, rather it the burden is on the Examiner to establish that the '966 patent in fact enabled that claimed method. Furthermore, Applicant argues in conjunction of case law that to anticipate under section 102, a prior art reference must disclose each and every limitation of the claimed invention, must be enabling, and must describe the claimed invention sufficiently to have placed it in the possession of a person of ordinary skill in the field of the invention. Applicant argues that the '966 patent does not specifically describe mAb's that target amino acid residues 91-96 of figure 15 in the treatment of arthritis to obtain the clinical endpoint of a decrease in arthritic score of about 65% or greater when compared to a control antibody treated subject.

In response to Applicant argument that the reference is could not target amino acid residues 91-96 of Figure 15 to provide a decrease in arthritic score of about 65% or greater when compared to a control antibody treated subject and that the reference is not enabling, but had not provided any objective evidence to support these assertions. Whether the rejection is based on "inherence" under 35 U.S.C. § 102 or prima facie obviousness under 35 U.S.C. § 103, jointly or alternatively, the burden of proof is the same and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. Examiner properly shifted burden to applicant to establish, through objective evidence, that the method using the antibody of invention differ in unobvious manner from those of the prior art references. Ex parte Phillips, 28 USPQ2d 1302 (BPAI 1993). Here, applicant has not provided any objective evidence to support the difference between the prior art and instant method. The record does not contain sufficient objective evidence that the referenced antibodies differ in any significant manner from that claimed.

Furtherr, the mechanism of action disclosed by the prior art does not preclude that the methods and compositions of '966 patent inherently would have had the properties recited in the claims because compositions comprising the same antibodies are administered to the same patients to treat the same type of arthritis condition to achieve the same result, that is, treating patients with arthritis. Regarding binding to epitope comprising amino acid residues 91-96 of Figure 15, given the high sequence identity between the referenced and claimed VLA-1 polypeptide; the referenced antibodies would have the inherent property of binding epitope comprising amino acid residues 91-96 in the absence of objective evidence to the contrary.

Applicant argues in conjunction with case laws that Applicants have not merely defined advantageous clinical end points within a treatment regiment specified by '966 patent. Instead, the invention of the pending claims utilizes mAb's that target amino acid residues 91-96 of Figure 15 in the treatment of arthritis to obtain the clinical endpoint of a decrease in arthritic score of about 65% or greater when compared to a control antibody treated subject. Applicant argues that there is no inherent anticipation in this instance. Applicant argues that the claimed novel method of treatment is patentably distinguishable from the '966 patent disclosure that mAb 1B3.1 reacts with T cells which have been activated from prolonged periods , both in vitro and in vivo.

In response to applicant's argument that there is no inherent anticipation in this instance. A recitation of (that the antibody, capable of binding an epitope of VLA-1 wherein the epitope comprises amino acid residues 91-96 of Figure 15) must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use "a decrease in arthritic score of about 65% or greater when compared to a control antibody treated subject", then it meets the claim. For example in Atlas Powder Co. V. IRECO, 51 USPQ2d 1943 (Fed. Cir. 1999); the following was noted. "Artisans of ordinary skill may not recognize the inherent characteristics or functioning of the prior art. However, the discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer. " The Court further held that "this same reasoning holds true when it is not a property but an ingredient which is inherently contained in the prior art". See MPEP 2112.02. Also, see Bristol-Myers Squibb Co. v. Ben Venue Laboratories, Inc. 58 USPQ2d 1508 (CA FC 2001); Ex parte Novitski 26 USPQ 1389 (BPAI 1993); Mehl Biophile International Corp. V. Milgraum, 52 USPQ2d 1303 (Fed. Cir. 1999); Atlas Powder Co. V. IRECO, 51 USPQ2d 1943 (Fed. Cir. 1999).

Further, applicant has not distinguished how administering an effective amount of 1B3.1 antibody to the referenced patients is distinguished over the claimed methods, which appear to rely upon the same active ingredient being administered to the same patient population to reduce collagen binding to VLA-1.

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 1-7 stand rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,788,966 (IDS Ref. No. AA), in view of Riikonen et al (Biochemical and Biophysical Research Communication 209:205-212, 1995) and Fabbri et al (IDS Ref. No. CB) for the same reasons set forth in the previous Office Action, paper No. 6, mailed 2 11 03.

Applicant's arguments, filed 4 29 03 (Paper No. 8), have been fully considered, but have not been found convincing.

Applicant argues that the '966 patent, Riikonen or Fabbri do not disclose that the FB12 mAb will bind to an epitope of VLA-1 comprising amino acid residues 91-96 of Figure 15 to provide a decrease in arthritic score of about 65% or greater when compared to a control antibody treated subject. Applicant further argues that when the references viewed collectively, the '966 patent description of mAb 1B3.1 reactions with T cells, Fabbri's disclosure that the FB12 mAb blocks adhesion of activated T lymphocytes to fibronectin and Riikonen's discloses that the mAb SR-84 blocks the function of $\alpha 1\beta 1$ integrin describe the behavior of three different mAbs under different experimental conditions. Applicant argues that those references do not specify the use of mAb's that target amino acid residue 91-96 of Figure 15 in the treatment of arthritis to obtain the clinical endpoint of a decrease in arthritic score of about 65% or greater when compared to a control antibody treated subject.

Contrary to Applicant assertions that the '966 patent teaches that the 1B3.1 antibody inhibits collagen binding to VLA-1. Similarly, Riikonen's mAb SR-84 also blocks collagen and laminin binding the $\alpha 1\beta 1$ (VLA-1) and Fabbri's FB12 antibodies inhibits collagen, laminin and fibronectin binding to VLA-1.

Applicant argues that there must be a rigorous showing of a clear and particular suggestion, teaching or motivation to combine the references relied upon. Applicant urges that the combination not be motivated by impermissible hindsight. Applicant submits that there must be a particular showing that one of ordinary skill in the art would have believed there was a

reasonable likelihood of success that the suggested combination of references would work to yield the claimed invention. Applicant argues that the Examiner has failed to provide a rigorous showing of a clear and particular suggestion, teaching, or motivation to combine the references to yield the methods of claims 1-7.

The combined teachings particularly Fabbri *et al* provide clear direction, motivation and expectation of success in treating arthritis with $\alpha 1\beta 1$-specific antibodies. There is no evidence that the method of treatment described in the instant claims would differ in an unexpected manner from those described in the references.

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that references cannot be arbitrarily combined and that there must be some reason why one skilled in the art would be motivated to make the proposed combination of primary and secondary references. In re Nomiya, 184 USPQ 607 (CPA 1975). However, there is no requirement that a motivation to make the modification be expressly articulated. The test for combining references is what the combination of disclosures taken as a whole would suggest to one of ordinary skill in the art . In re McLaughlin, 170 USPQ 209 (CCPA 1971). References are evaluated by what they suggest to one versed in the art, rather than by their specific disclosures. In re Bozek, 163 USPQ 545 (CCPA 1969).

Further the motivation to combine can arise from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combine for their common known purpose. Section MPEP 2144.07.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. In re McLaughlin , 170 USPQ 209 (CCPA 1971).

11. Claims 1-7 stand rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,788,966 (IDS Ref. No. AA), in view of Riikonen et al (Biochemical and Biophysical Research Communication 209:205-212, 1995) for the same reasons set forth in the previous Office Action, paper No. 6, mailed 2/11/03.

Applicant's arguments, filed 4/29/03 (Paper No. 8), have been fully considered, but have not been found convincing.

Applicant has presented the same arguments above under claim rejections: 35 U.S.C § 103 and Examiner rebuttals are same as addressed above in section 10.

12. No claim allowed

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad, whose telephone number is (703) 306-3472. The examiner can normally be reached Monday to Friday from 8:00 to 4:30. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Maher Haddad, Ph.D.
Patent Examiner
Technology Center 1600
July 14, 2003

CHRISTINA CHAN
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